

Express Mail Label No.: EK611913861US
Date of Deposit: February 2, 2001

PATENT APPLICATION
Atty Docket No. 15966-577A CIP3 (Cura-77A CIP3)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Shimkets *et al.*
ASSIGNEE: CuraGen Corporation
SERIAL NUMBER: 09/688,312
FILING DATE: October 13, 2000
FOR: GROWTH FACTOR POLYPEPTIDES AND NUCLEIC ACIDS ENCODING SAME

EXAMINER: Not Yet Assigned

ART UNIT: Not Yet Assigned

February 2, 2001
Boston, Massachusetts

Assistant Commissioner for Patents
Washington, D.C. 20231



INFORMATION DISCLOSURE STATEMENT

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, Applicants hereby make of record the documents listed below and on the attached modified Form PTO-1449 (submitted in duplicate) in the above-identified application, copies of which are submitted herewith. The order of presentation of the references should not be construed as an indication of the importance of the references.

U.S. Patent Documents:

A1	4,816,567	3/28/89	Cabilly, et al.
A2	5,225,539	7/6/93	Winter
A3	5,545,807	8/13/96	Surani, et al.
A4	5,545,806	8/13/96	Lonberg, et al.
A5	5,569,825	10/29/96	Lonberg, et al.
A6	5,625,126	4/29/97	Lonberg, et al.
A7	5,939,598	8/17/99	Kucherlapati, et al.
A8	5,916,771	6/29/99	Hori, et al.

Foreign Patent Documents:

B1	WO	96/41892	Mileham, et al.	12/27/96
B2	WO	00/27879	Eriksson, et al.	5/18/00
B3	WO	94/02602	Kuncherlapati, et al.	2/3/94
B4	WO	96/33735	Kuncherlapati, et al.	10/31/96
B5	WO	96/34096	Kuncherlapati, et al.	10/31/96
B6	WO	99/53049	Davis, et al.	10/21/99

Other Prior Art – Non Patent Literature Documents:

C1 Alon, T., I. Hemo, et al. (1995). "Vascular endothelial growth factor acts as a survival factor for newly formed retinal vessels and has implications for retinopathy of prematurity." Nat Med 1(10): 1024-8.

- C2 Athanassiades, A. and P. K. Lala (1998). "Role of placenta growth factor (PIGF) in human extravillous trophoblast proliferation, migration and invasiveness." Placenta 19(7): 465-73.
- C3 Bellamy, W. T., L. Richter, et al. (1999). "Expression of vascular endothelial growth factor and its receptors in hematopoietic malignancies." Cancer Res 59(3): 728-33.
- C4 Betsholtz, C., A. Johnsson, et al. (1986). "cDNA sequence and chromosomal localization of human platelet-derived growth factor A-chain and its expression in tumour cell lines." Nature 320(6064): 695-9.
- C5 Bonthron, D. T., C. C. Morton, et al. (1988). "Platelet-derived growth factor A chain: gene structure, chromosomal location, and basis for alternative mRNA splicing." Proc Natl Acad Sci U S A 85(5): 1492-6.
- C6 Carmeliet, P., M. G. Lampugnani, et al. (1999). "Targeted deficiency or cytosolic truncation of the VE-cadherin gene in mice impairs VEGF-mediated endothelial survival and angiogenesis." Cell 98(2): 147-57.
- C7 Collins, T., D. Ginsburg, et al. (1985). "Cultured human endothelial cells express platelet-derived growth factor B chain: cDNA cloning and structural analysis." Nature 316(6030): 748-50.
- C8 Cote, R. M., DM; Houghton, AN; Beattie, EJ; Oettgen, HF; Old, LJ (1983). "Generation of human monoclonal antibodies reactive with cellular antigens." Proc. Natl. Acad. Sci. USA 80: 2026-2030.
- C9 Dalla-Favera, R., E. P. Gelmann, et al. (1981). "A human onc gene homologous to the transforming gene (v-sis) of simian sarcoma virus." Nature 292(5818): 31-5.
- C10 Doolittle, R. F., M. W. Hunkapiller, et al. (1983). "Simian sarcoma virus onc gene, v-sis, is derived from the gene (or genes) encoding a platelet-derived growth factor." Science 221(4607): 275-7.
- C11 Ferrara, N. (1999). "Vascular endothelial growth factor: molecular and biological aspects." Curr Top Microbiol Immunol 237: 1-30.
- C12 Fishwild, D. M., S. L. O'Donnell, et al. (1996). "High-avidity human IgG kappa monoclonal antibodies from a novel strain of minilocus transgenic mice [see comments]." Nat Biotechnol 14(7): 845-51.
- C13 Folkman, J. (1995). "Angiogenesis in cancer, vascular, rheumatoid and other disease." Nat Med 1(1): 27-31.
- C14 Gerber, H. P., A. McMurtrey, et al. (1998). "Vascular endothelial growth factor regulates endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway. Requirement for Flk-1/KDR activation." J Biol Chem 273(46): 30336-43.
- C15 Gerber, H. P., V. Dixit, et al. (1998). "Vascular endothelial growth factor induces expression of the antiapoptotic proteins Bcl-2 and A1 in vascular endothelial cells." J Biol Chem 273(21): 13313-6.
- C16 Hamada, et al., 2000 "A novel gene derived from developing spinal cords, SCDGF, is a unique member of the PDGF/BEFF family." FEBS Lett. 475(2): 970-102. GenBank Accession Number: **BAB03265**
- C17 Helmlinger, G., M. Endo, et al. (2000). "Formation of endothelial cell networks." Nature 405(6783): 139-41.
- C18 Hermansson, M., M. Nister, et al. (1988). "Endothelial cell hyperplasia in human glioblastoma: coexpression of mRNA for platelet-derived growth factor (PDGF) B chain and PDGF receptor suggests autocrine growth stimulation." Proc Natl Acad Sci U S A 85(20): 7748-52.
- C19 Holash, J., P. C. Maisonpierre, et al. (1999). "Vessel cooption, regression, and growth in tumors mediated by angiopoietins and VEGF." Science 284(5422): 1994-8.
- C20 Hoogenboom, H. R. and G. Winter (1992). "By-passing immunisation. Human antibodies from synthetic repertoires of germline VH gene segments rearranged in vitro." J Mol Biol 227(2): 381-8.
- C21 Hopp, T. P. and K. R. Woods (1981). "Prediction of protein antigenic determinants from amino acid sequences." Proc Natl Acad Sci U S A 78(6): 3824-8.
- C22 Jones, P. T., P. H. Dear, et al. (1986). "Replacing the complementarity-determining regions in a human antibody with those from a mouse." Nature 321(6069): 522-5.
- C23 Josephs, S. F., C. Guo, et al. (1984). "Human-proto-oncogene nucleotide sequences corresponding to the transforming region of simian sarcoma virus." Science 223(4635): 487-91.
- C24 Katoh, M. and M. Terada (1996). "Overexpression of bone morphogenetic protein (BMP)-4 mRNA in gastric cancer cell lines of poorly differentiated type." J Gastroenterol 31(1): 137-9.
- C25 Kelly, J. D., E. W. Raines, et al. (1985). "The B chain of PDGF alone is sufficient for mitogenesis." Embo J 4(13A): 3399-405.
- C26 Kessler, E., K. Takahara, et al. (1996). "Bone morphogenetic protein-1: the type I procollagen C-proteinase [see comments]." Science 271(5247): 360-2.
- C27 Kohler, G. and C. Milstein (1975). "Continuous cultures of fused cells secreting antibody of predefined specificity." Nature 256(5517): 495-7.
- C28 Kozbor, D. and J. Roder (1983). "The production of monoclonal antibodies from human lymphocytes." Immunology Today 4(3): 72-79.
- C29 Kozbor, D., P. Tripputi, et al. (1984). "A human hybrid myeloma for production of human monoclonal antibodies." J Immunol 133(6): 3001-5.
- C30 Kyte, J. and R. F. Doolittle (1982). "A simple method for displaying the hydropathic character of a protein." J Mol Biol 157(1): 105-32.

APPLICANTS: Shimkets *et al.*
U.S.S.N.: 09/688,312

- C31 Li, et al., 2000 "PDGF-C is a novel protease-activated ligand for the PDGF alpha receptor." *Nat. Cell Biol.* Direct Submission. GenBank Accession Number: **AAF80597**
- C32 Li, J. M., J. S. Han, et al. (1999). "A novel gene delivery system targeting cells expressing VEGF receptors." *Cell Res* 9(1): 11-25.
- C33 Lonberg, N. and D. Huszar (1995). "Human antibodies from transgenic mice." *Int Rev Immunol* 13(1): 65-93.
- C34 Lonberg, N., L. D. Taylor, et al. (1994). "Antigen-specific human antibodies from mice comprising four distinct genetic modifications [see comments]." *Nature* 368(6474): 856-9.
- C35 Maeno, et al., 1993 "Cloning and expression of cDNA encoding *Zenopus laevis* bone morphogenetic protein-1 during early embryonic development." *Gene* 134(2): 257-261. GenBank Accession Number: **P98070**
- C36 Marks, J. D., A. D. Griffiths, et al. (1992). "By-passing immunization: building high affinity human antibodies by chain shuffling." *Biotechnology (N Y)* 10(7): 779-83.
- C37 Marks, J. D., H. R. Hoogenboom, et al. (1991). "By-passing immunization. Human antibodies from V-gene libraries displayed on phage." *J Mol Biol* 222(3): 581-97.
- C38 Marzo, I., C. Brenner, et al. (1998). "The central role of the mitochondrial megachannel in apoptosis: evidence obtained with intact cells, isolated mitochondria, and purified protein complexes." *Biomed Pharmacother* 52(6): 248-51.
- C39 Masood, R., J. Cai, et al. (1997). "Vascular endothelial growth factor/vascular permeability factor is an autocrine growth factor for AIDS-Kaposi sarcoma." *Proc Natl Acad Sci U S A* 94(3): 979-84.
- C40 Millauer, B., L. K. Shawver, et al. (1994). "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant." *Nature* 367(6463): 576-9.
- C41 Morrison, S. L. (1994). "Immunology. Success in specification [news; comment]." *Nature* 368(6474): 812-3.
- C42 Munson, P. J. and D. Rodbard (1980). "Ligand: a versatile computerized approach for characterization of ligand-binding systems." *Anal Biochem* 107(1): 220-39.
- C43 Neuberger, M. (1996). "Generating high-avidity human Mabs in mice [news; comment]." *Nat Biotechnol* 14(7): 826.
- C44 Poltorak, Z., T. Cohen, et al. (1997). "VEGF145, a secreted vascular endothelial growth factor isoform that binds to extracellular matrix." *J Biol Chem* 272(11): 7151-8.
- C45 Riechmann, L., M. Clark, et al. (1988). "Reshaping human antibodies for therapy." *Nature* 332(6162): 323-7.
- C46 Risau, W. (1995). "Differentiation of endothelium." *Faseb J* 9(10): 926-33.
- C47 Risau, W. and I. Flamme (1995). "Vasculogenesis." *Annu Rev Cell Dev Biol* 11: 73-91.
- C48 Rocchigiani, et al., 1998 "Human RIGF: cloning, gene structure, and mapping to chromosome Xp22.1 between the PIGA and the GRPR genes." *Genomics* 47: 207-216. GenBank Accession Number: **O43915**
- C49 Romashkova, J. A. and S. S. Makarov (1999). "NF-kappaB is a target of AKT in anti-apoptotic PDGF signalling [see comments]." *Nature* 401(6748): 86-90.
- C50 Shimizu, A., K. P. O'Brien, et al. (1999). "The dermatofibrosarcoma protuberans-associated collagen type Ialpha1/platelet-derived growth factor (PDGF) B-chain fusion gene generates a transforming protein that is processed to functional PDGF- BB." *Cancer Res* 59(15): 3719-23.
- C51 Simon, M. P., F. Pedetour, et al. (1997). "Deregulation of the platelet-derived growth factor B-chain gene via fusion with collagen gene COL1A1 in dermatofibrosarcoma protuberans and giant-cell fibroblastoma." *Nat Genet* 15(1): 95-8.
- C52 Speirs, V. and S. L. Atkin (1999). "Production of VEGF and expression of the VEGF receptors Flt-and KDR in primary cultures of epithelial and stromal cells derived from breast tumours." *Br J Cancer* 80(5-6): 898-903.
- C53 Tischer, E., R. Mitchell, et al. (1991). "The human gene for vascular endothelial growth factor. Multiple protein forms are encoded through alternative exon splicing." *J Biol Chem* 266(18): 11947-54.
- C54 Tsai, et al., 1998 "Fallotein, a novel growth factor like gene identified in human uterus." GenBank Accession Number: **Q9UL22**
- C55 Tsai, et al., 1999 "cDNA cloning of fallotein from mouse ovary." GenBank Accession Number: **Q9QY71**
- C56 Tsai, et al., 2000 "Identification of a novel platelet-derived growth factor-like gene, fallotein, in the human reproductive tract." *Biochim. Biophys. Acta* 1492(1) 196-202. GenBank Accession Number: **AAF00049**
- C57 Tsai, et al., 2000 "Identification of a novel platelet-derived growth factor-like gene, fallotein, in the human reproductive tract." *Biochim. Biophys. Acta* 1492(1) 196-202. GenBank Accession Number: **AF091434**
- C58 Verhoeyen, M., C. Milstein, et al. (1988). "Reshaping human antibodies: grafting an antilysozyme activity." *Science* 239(4847): 1534-6.
- C59 Warren, R. S., H. Yuan, et al. (1995). "Regulation by vascular endothelial growth factor of human colon cancer tumorigenesis in a mouse model of experimental liver metastasis." *J Clin Invest* 95(4): 1789-97.

APPLICANTS: Shimkets *et al.*
U.S.S.N.: 09/688,312

- C60 Wilcox, J. N., K. M. Smith, et al. (1988). "Platelet-derived growth factor mRNA detection in human atherosclerotic plaques by in situ hybridization." J Clin Invest 82(3): 1134-43.
- C61 Wilkinson, D. 2000. The Scientist. 14(8): 25-28.
- C62 Wozney, et al., 1988 "Novel regulators of bone formation: molecular clones and activities." Science 242(4885): 1528-1534. GenBank Accession Number: **PIR-ID:A58788**
- C63 Wozney, J. M., V. Rosen, et al. (1988). "Novel regulators of bone formation: molecular clones and activities." Science 242(4885): 1528-34.
- C64 Yamada, et al., "Molecular cloning of a novel vascular endothelial growth factor, VEGF-D." Genomics: 42:483-488. GenBank Accession Number: **O35251**
- C65 Yoshikawa, H., K. Takaoka, et al. (1985). "Clinical significance of bone morphogenetic activity in osteosarcoma. A study of 20 cases." Cancer 56(7): 1682-7.
- C66 Yuan, F., Y. Chen, et al. (1996). "Time-dependent vascular regression and permeability changes in established human tumor xenografts induced by an anti-vascular endothelial growth factor/vascular permeability factor antibody." Proc Natl Acad Sci U S A 93(25): 14765-70.

This Information Disclosure Statement is being been filed:

- ☒ within three months of the filing date of the National Application;
- ☐ within three months of the filing date of the entry of the National Stage, as set forth in 37 C.F.R. §1.491, in an International Application; or
- ☐ before the mailing date of a first Office Action on the merits in the above-identified case.

Accordingly, no fee or certification is required. 37 C.F.R. §1.97

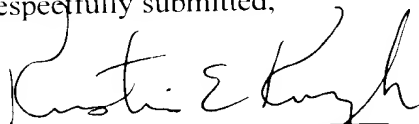
A copy of each of the above-identified information is enclosed unless otherwise indicated on the attached Form PTO-1449 (modified). It is respectfully requested that the Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims, and signs the enclosed form PTO-1449 to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application.

By submitting this Information Disclosure Statement, the Applicant makes no representation that: (1) a search has been performed, of the extent of any search performed, or that more relevant information does not exist; (2) the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b); and (3) the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

APPLICANTS: Shimkets *et al.*
U.S.S.N.: 09/688,312

Notwithstanding any statements by the Applicant, the Examiner is urged to form his/her own conclusion regarding the relevance of the cited information. An early and favorable action is hereby requested. Please charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. CURA-77A CIP (15966-577A CIP3).

Respectfully submitted,



Ivor R. Elrifi, Reg. No. 39,529
Kristin E. Konzak, Reg. No. 44,848
Attorney/Agent for Applicants
MINTZ, LEVIN
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000
Fax: (617) 542-2241

Dated: February 2, 2001

TRADOCS:1430485.1(%NRP01!.DOC)

Express Mail Label No.: EK611913861US
Date of Deposit: February 2, 2001

PATENT APPLICATION
Attorney Docket No.: 15966-577A CIP3 (Cura-77A CIP3)

Page 1 of 4

Please type a plus sign (+) in this box



PTO/S&P Form 1001
Approved for use through 9/30/00 OMB 065-0187
Patent and Trademark Office U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Modified Form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)	Application Number	TBA - filed herewith
	Filing Date	
	First Named Inventor	Shimkets, et al.
	Group Art Unit	Not Yet Assigned
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	15966-577A CIP3 (CURA-77A CIP3)

U.S. PATENT DOCUMENTS							
Exam Initials	Cite No.	U.S. Patent Document No.	Issue Date	Name of Patentee(s) or Applicant(s)	Class	Sub Class	Filing Date If Appropriate
	*A1	4,816,567	3/28/89	Cabilly, et al.			
	*A2	5,225,539	7/6/93	Winter			
	*A3	5,545,807	8/13/96	Surani, et al.			
	*A4	5,545,806	8/13/96	Lonberg, et al.			
	*A5	5,569,825	10/29/96	Lonberg, et al.			
	*A6	5,625,126	4/29/97	Lonberg, et al.			
	*A7	5,939,598	8/17/99	Kucherlapati, et al.			
	*A8	5,916,771	6/29/99	Hori, et al.			

FOREIGN PATENT DOCUMENTS						
Exam Initials	Cite No.	Foreign Patent Document Office Number	Name of Patentee(s) or Applicant(s)	Date of Publication	Translation Yes No	
	*B1	WO 96/41892	Milham, et al.	12/27/96		
	*B2	WO 00/27879	Eriksson, et al.	5/18/00		
	*B3	WO 94/02602	Kucherlapati, et al.	2/3/94		
	*B4	WO 96/33735	Kucherlapati, et al.	10/31/96		
	*B5	WO 96/34096	Kucherlapati, et al.	10/31/96		
	*B6	WO 99/53049	Davis, et al.	10/21/99		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	*C1	Alon, et al. (1995). "Vascular endothelial growth factor acts as a survival factor for newly formed retinal vessels and has implications for retinopathy of prematurity." <u>Nat Med</u> 1(10): 1024-8.
	*C2	Athanassiades and Lala (1998). "Role of placenta growth factor (PlGF) in human extravillous trophoblast proliferation, migration and invasiveness." <u>Placenta</u> 19(7): 465-73.
	*C3	Bellamy, et al. (1999). "Expression of vascular endothelial growth factor and its receptors in hematopoietic malignancies." <u>Cancer Res</u> 59(3): 728-33.
	*C4	Betsholtz, et al. (1986). "cDNA sequence and chromosomal localization of human platelet-derived growth factor A-chain and its expression in tumour cell lines." <u>Nature</u> 320(6064): 695-9.
	*C5	Bonthron, et al. (1988). "Platelet-derived growth factor A chain: gene structure, chromosomal location, and basis for alternative mRNA splicing." <u>Proc Natl Acad Sci U S A</u> 85(5): 1492-6.
	*C6	Carmeliet, et al. (1999). "Targeted deficiency or cytosolic truncation of the VE-cadherin gene in mice impairs VEGF-mediated endothelial survival and angiogenesis." <u>Cell</u> 98(2): 147-57.

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	*C7	Collinset al. (1985). "Cultured human endothelial cells express platelet-derived growth factor B chain: cDNA cloning and structural analysis." <u>Nature</u> 316(6030): 748-50.
	*C8	Cote, et al. (1983). "Generation of human monoclonal antibodies reactive with cellular antigens." <u>Proc. Natl. Acad. Sci. USA</u> 80: 2026-2030.
	*C9	Dalla-Favera, et al. (1981). "A human onc gene homologous to the transforming gene (v-sis) of simian sarcoma virus." <u>Nature</u> 292(5818): 31-5.
	*C10	Doolittle, et al. (1983). "Simian sarcoma virus onc gene, v-sis, is derived from the gene (or genes) encoding a platelet-derived growth factor." <u>Science</u> 221(4607): 275-7.
	*C11	Ferrara, (1999). "Vascular endothelial growth factor: molecular and biological aspects." <u>Curr Top Microbiol Immunol</u> 237: 1-30.
	*C12	Fishwild, et al. (1996). "High-avidity human IgG kappa monoclonal antibodies from a novel strain of minilocus transgenic mice [see comments]." <u>Nat Biotechnol</u> 14(7): 845-51.
	*C13	Folkman, (1995). "Angiogenesis in cancer, vascular, rheumatoid and other disease." <u>Nat Med</u> 1(1): 27-31.
	*C14	Gerber, et al. (1998). "Vascular endothelial growth factor regulates endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway. Requirement for Flk-1/KDR activation." <u>J Biol Chem</u> 273(46): 30336-43.
	*C15	Gerber et al. (1998). "Vascular endothelial growth factor induces expression of the antiapoptotic proteins Bcl-2 and A1 in vascular endothelial cells." <u>J Biol Chem</u> 273(21): 13313-6.
	*C16	Hamada, et al., 2000 "A novel gene derived from developing spinal cords, SCDGF, is a unique member of the PDGF/BEFF family." <u>FEBS Lett.</u> 475(2): 970-102. GenBank Accession Number: BAB03265
	*C17	Helmlinger, et al. (2000). "Formation of endothelial cell networks." <u>Nature</u> 405(6783): 139-41.
	*C18	Hermansson, et al. (1988). "Endothelial cell hyperplasia in human glioblastoma: coexpression of mRNA for platelet-derived growth factor (PDGF) B chain and PDGF receptor suggests autocrine growth stimulation." <u>Proc Natl Acad Sci U S A</u> 85(20): 7748-52.
	*C19	Holash, et al. (1999). "Vessel cooption, regression, and growth in tumors mediated by angiopoietins and VEGF." <u>Science</u> 284(5422): 1994-8.
	*C20	Hoogenboom and Winter (1992). "By-passing immunisation. Human antibodies from synthetic repertoires of germline VH gene segments rearranged in vitro." <u>J Mol Biol</u> 227(2): 381-8.
	*C21	Hopp and Woods (1981). "Prediction of protein antigenic determinants from amino acid sequences." <u>Proc Natl Acad Sci U S A</u> 78(6): 3824-8.
	*C22	Jones, et al. (1986). "Replacing the complementarity-determining regions in a human antibody with those from a mouse." <u>Nature</u> 321(6069): 522-5.
	*C23	Josephs, et al. (1984). "Human proto-oncogene nucleotide sequences corresponding to the transforming region of simian sarcoma virus." <u>Science</u> 223(4635): 487-91.
	*C24	Katoh and Terada (1996). "Overexpression of bone morphogenic protein (BMP)-4 mRNA in gastric cancer cell lines of poorly differentiated type." <u>J Gastroenterol</u> 31(1): 137-9.
	*C25	Kelly, et al. (1985). "The B chain of PDGF alone is sufficient for mitogenesis." <u>Embo J</u> 4(13A): 3399-405.
	*C26	Kessler, et al. (1996). "Bone morphogenetic protein-1: the type I procollagen C-proteinase [see comments]." <u>Science</u> 271(5247): 360-2.
	*C27	Kohler and Milstein (1975). "Continuous cultures of fused cells secreting antibody of predefined specificity." <u>Nature</u> 256(5517): 495-7.
	*C28	Kozbor and Roder (1983). "The production of monoclonal antibodies from human lymphocytes." <u>Immunology Today</u> 4(3): 72-79.
	*C29	Kozbor, et al. (1984). "A human hybrid myeloma for production of human monoclonal antibodies." <u>J Immunol</u> 133(6): 3001-5.
	*C30	Kyte and Doolittle (1982). "A simple method for displaying the hydropathic character of a protein." <u>J Mol Biol</u> 157(1): 105-32.
	*C31	Li, et al., 2000 "PDGF-C is a novel protease-activated ligand for the PDGF alpha receptor." <u>Nat. Cell Biol. Direct Submission.</u> GenBank Accession Number: AAF80597

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	*C32	Liet al. (1999). "A novel gene delivery system targeting cells expressing VEGF receptors." <u>Cell Res</u> 9(1): 11-25.
	*C33	Lonberg and Huszar (1995). "Human antibodies from transgenic mice." <u>Int Rev Immunol</u> 13: 65-93.
	*C34	Lonberg, et al. (1994). "Antigen-specific human antibodies from mice comprising four distinct genetic modifications [see comments]." <u>Nature</u> 368(6474): 856-9.
	*C35	Maeno, et al., 1993 "Cloning and expression of cDNA encoding <i>Zenopus laevis</i> bone morphogenetic protein-1 during early embryonic development." <u>Gene</u> 134(2): 257-261. GenBank Accession Number: P98070
	*C36	Marks, et al. (1992). "By-passing immunization: building high affinity human antibodies by chain shuffling." <u>Biotechnology (N Y)</u> 10(7): 779-83.
	*C37	Marks, et al. (1991). "By-passing immunization. Human antibodies from V-gene libraries displayed on phage." <u>J Mol Biol</u> 222(3): 581-97.
	*C38	Marzo, et al. (1998). "The central role of the mitochondrial megachannel in apoptosis: evidence obtained with intact cells, isolated mitochondria, and purified protein complexes." <u>Biomed Pharmacother</u> 52(6): 248-51.
	*C39	Masood, et al. (1997). "Vascular endothelial growth factor/vascular permeability factor is an autocrine growth factor for AIDS-Kaposi sarcoma." <u>Proc Natl Acad Sci U S A</u> 94(3): 979-84.
	*C40	Millauer, et al. (1994). "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant." <u>Nature</u> 367(6463): 576-9.
	*C41	Morrison. (1994). "Immunology. Success in specification [news: comment]." <u>Nature</u> 368(6474): 812-3.
	*C42	Munson and Rodbard (1980). "Ligand: a versatile computerized approach for characterization of ligand-binding systems." <u>Anal Biochem</u> 107(1): 220-39.
	*C43	Neuberger, (1996). "Generating high-avidity human Mabs in mice [news; comment]." <u>Nat Biotechnol</u> 14(7): 826.
	*C44	Poltorak, et al. (1997). "VEGF145, a secreted vascular endothelial growth factor isoform that binds to extracellular matrix." <u>J Biol Chem</u> 272(11): 7151-8.
	*C45	Riechmann, et al. (1988). "Reshaping human antibodies for therapy." <u>Nature</u> 332(6162): 323-7.
	*C46	Risau, (1995). "Differentiation of endothelium." <u>Faseb J</u> 9(10): 926-33.
	*C47	Risau, and Flamme (1995). "Vasculogenesis." <u>Annu Rev Cell Dev Biol</u> 11: 73-91.
	*C48	Rocchigiani, et al., 1998 "Human FIGF: cloning, gene structure, and mapping to chromosome Xp22.1 between the FIGA and the GRPR genes." <u>Genomics</u> 47: 207-216. GenBank Accession Number: O43915
	*C49	Romashkova and Makarov (1999). "NF-kappaB is a target of AKT in anti-apoptotic PDGF signalling [see comments]." <u>Nature</u> 401(6748): 86-90.
	*C50	Shimizu, et al. (1999). "The dermatofibrosarcoma protuberans-associated collagen type Ialpha1/platelet-derived growth factor (PDGF) B-chain fusion gene generates a transforming protein that is processed to functional PDGF- BB." <u>Cancer Res</u> 59(15): 3719-23.
	*C51	Simon, et al. (1997). "Deregulation of the platelet-derived growth factor B-chain gene via fusion with collagen gene COL1A1 in dermatofibrosarcoma protuberans and giant-cell fibroblastoma." <u>Nat Genet</u> 15(1): 95-8.
	*C52	Speirs and Atkin (1999). "Production of VEGF and expression of the VEGF receptors Flt-and KDR in primary cultures of epithelial and stromal cells derived from breast tumours." <u>Br J Cancer</u> 80(5-6): 898-903.
	*C53	Tischer, et al. (1991). "The human gene for vascular endothelial growth factor. Multiple protein forms are encoded through alternative exon splicing." <u>J Biol Chem</u> 266(18): 11947-54.
	*C54	Tsai, et al., 1998 "Fallotein, a novel growth factor like gene identified in human uterus." GenBank Accession Number: Q9UL22
	*C55	Tsai, et al., 1999 "cDNA cloning of fallotein from mouse ovary." GenBank Accession Number: Q9QY71

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	*C56	Tsai, et al., 2000 "Identification of a novel platelet-derived growth factor-like gene, fallotein, in the human reproductive tract." <i>Biochim. Biophys. Acta</i> 1492(1) 196-202. GenBank Accession Number: AAF00049
	*C57	Tsai, et al., 2000 "Identification of a novel platelet-derived growth factor-like gene, fallotein, in the human reproductive tract." <i>Biochim. Biophys. Acta</i> 1492(1) 196-202. GenBank Accession Number: AF091434
	*C58	Verhoeven, et al. (1988). "Reshaping human antibodies: grafting an antilysozyme activity." <i>Science</i> 239(4847): 1534-6.
	*C59	Warren, et al. (1995). "Regulation by vascular endothelial growth factor of human colon cancer tumorigenesis in a mouse model of experimental liver metastasis." <i>J Clin Invest</i> 95(4): 1789-97.
	*C60	Wilcox, et al. (1988). "Platelet-derived growth factor mRNA detection in human atherosclerotic plaques by in situ hybridization." <i>J Clin Invest</i> 82(3): 1134-43.
	*C61	Wilkinson, D. 2000. <i>The Scientist</i> 14(8): 25-28.
	*C62	Wozney, et al., 1988 "Novel regulators of bone formation: molecular clones and activities." <i>Science</i> 242(4885): 1528-1534. GenBank Accession Number: PIR-ID:A58788
	*C63	Wozney, et al. (1988). "Novel regulators of bone formation: molecular clones and activities." <i>Science</i> 242(4885): 1528-34.
	*C64	Yamada, et al., "Molecular cloning of a novel vascular endothelial growth factor, VEGF-D." <i>Genomics</i> 42:483-488. GenBank Accession Number: O35251
	*C65	Yoshikawa et al. (1985). "Clinical significance of bone morphogenetic activity in osteosarcoma. A study of 20 cases." <i>Cancer</i> 56(7): 1682-7.
	*C66	Yuan, et al. (1996). "Time-dependent vascular regression and permeability changes in established human tumor xenografts induced by an anti-vascular endothelial growth factor/vascular permeability factor antibody." <i>Proc Natl Acad Sci U S A</i> 93(25): 14765-70.

* a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 09/688,312, filed December 26, 2000, and relied upon for an earlier filing date under 35 U.S.C. §120 (continuation-in-part).

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to applicant.

TRADOCS:1430486.1(%NRQ01!.DOC)